

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
15 July 2004 (15.07.2004)

PCT

(10) International Publication Number
WO 2004/058158 A3

(51) International Patent Classification⁷: **A61K 38/00**

(11) International Application Number:
PCT/US2003/040344

(22) International Filing Date:
20 December 2003 (20.12.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/415,139 20 December 2002 (20.12.2002) US

(71) Applicant: **THE JOHNS HOPKINS UNIVERSITY**
[US/US]; 100 N. Charles Street, 5th floor, Baltimore, MD
21201 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **KOVBASNJUK,**
Olga, N. [UA/US]; 7971 Brightmeadow Ct., Ellicott City,
MD 21043 (US). **DONOWOTZ, Mark** [US/US]; 4308
Greenway, Baltimore, MD 21218 (US).

(74) Agents: **ROSENFELD, Jennifer, K et al.;** Edwards &
Angell, LLP, P.O. Box 9169, Boston, MA 02209 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR,
CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN,
MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU,
SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (BW, GH,
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the international search report:
14 April 2005

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: TREATMENT OF METASTATIC CANCER WITH THE B-SUBUNIT OF SHIGA TOXIN

(57) Abstract: The present invention relates to compositions and methods for treating invasive or metastatic cancer, particularly metastatic colon cancer using the B-subunit of shiga toxin. The invention further provides methods of identifying compounds usefully for the treatment of invasive or metastatic cancer, particularly metastatic colon cancer.

WO 2004/058158 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/40344

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 38/00

US CL : 514/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/12

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LACASSE, E.C. et al. Shiga-Like Toxin purges Human Lymphoma From Bone Marrow of Severe Combined Immunodeficient Mice. Blood. September 01, 1996, Vol. 88. No. 5, pages 1561-1567, see abstract.	1, 3
X	MARCATO, P. et al. Cloned Shiga Toxin B Sununit Induces Apoptosis in Ramos Burkitt's Lymphoma B cells. Infection and Immunity. March 2002, Vol. 70. No. 3 pages 1279-1286, see abstract.	1, 3

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

11 January 2005 (11.01.2005)

Date of mailing of the international search report

09 FEB 2005

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Sheela J Huff

Telephone No. 571272-1600

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/40344

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claim Nos.: 4-12
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-3

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/US03/40344

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-3, drawn to method of preventing, reducing, or inhibiting invasiveness and metastasis by administering the B-subunit of Shiga Toxin.

Group II, claim(s) 13-17, drawn to method of identifying a compound capable of preventing, reducing or inhibiting tumor cells invasiveness and metastasis using cells that produce GB3.

The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Each of the methods of Groups I and II use products that differ structurally and functionally and this lack the same or corresponding special technical feature. The product used in Group I is a polypeptide and the product used in Group II is a cell.

Continuation of B. FIELDS SEARCHED Item 3:

STN adn WEST

search terms: shiga near2 toxin; b near2 subunit; tumour\$ or cancer\$ or tumor\$ or malignant\$ or neoplas\$